UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,341	10/20/2005	Jian Liu	421/67 PCT/US	2710

7590 11/02/2006

Arles A Taylor Jr
Jenkins Wilson & Taylor
Suite 1400 University Tower
3100 Tower Boulevard
Durham, NC 27707

EXAMINER	
SHEN, WU CHENG WINSTON	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 11/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/520,341	LIU ET AL.	
	Examiner	Art Unit	
	Wu-Cheng Winston Shen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-60* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-60 are pending in the instant application.

Election/Restrictions

2. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

I. Claims 1-4, drawn to an isolated and purified biologically active heparan sulfate 3-*O*-sulfotransferase 5 polypeptide, wherein the polypeptide comprises: (a) a polypeptide encoded by a nucleic acid sequence as set forth in SEQ ID NO 1; (b) a polypeptide encoded by a nucleic acid sequence having greater than 90% sequence identity to SEQ ID NO 1; (c) a polypeptide having an amino acid sequence as set forth in SEQ ID NO 2; (d) a polypeptide which is a biological equivalent of the polypeptide set forth in SEQ ID NO 2; (e) a polypeptide which is immunologically cross-reactive with an antibody which is immunoreactive with a polypeptide comprising part or all of the amino acids of SEQ ID NO 2; or (f) a polypeptide encoded by a nucleic acid molecule capable of hybridizing under

stringent conditions to a nucleic acid molecule comprising the nucleotides of SEQ ID NO 1, or a complement thereof.

II. Claims 5, drawn to an isolated and purified antibody capable of specifically binding to the polypeptide of an isolated and purified biologically active heparan sulfate 3-*O*-sulfotransferase 5 polypeptide,

III. Claims 6-12, drawn to an isolated and purified nucleic acid molecule encoding a biologically active heparan sulfate 8.O-sulfotransferase 5 polypeptide.

IV. Claim 13, drawn to a recombinant host cell comprising an isolated and purified nucleic acid molecule encoding a biologically active heparan sulfate 8.O-sulfotransferase 5 polypeptide

V. Claim 14, drawn to a transgenic non-human animal having incorporated into its genome a xenogeneic nucleic acid molecule encoding a biologically active heparan sulfate 3-*O*-sulfotransferase 5 polypeptide, the nucleic acid molecule being present in the genome in a copy number effective to confer expression in the animal of the heparan sulfate 3-*O*-sulfotransferase 5 polypeptide.

VI. Claim 15-16, drawn to a method of producing an antibody immunoreactive with a heparan sulfate 3-*O*-sulfotransferase 5 polypeptide, the method comprising: (i) transfecting a recombinant host cell with a nucleic acid molecule of claim 6, which encodes a heparan sulfate 3-*O*-sulfotransferase 5 polypeptide; (ii) culturing the host cell under conditions sufficient for expression of the polypeptide; (iii) recovering the polypeptide; and (iv) preparing an antibody to the polypeptide.

VII. Claim 17, drawn to a method of detecting a heparan sulfate 3-*O*-sulfotransferase polypeptide, the method comprising immunoreacting the polypeptide with an antibody prepared according the method of claim 15 to form an antibody-polypeptide conjugate; and detecting the conjugate.

VIII. Claim 18, drawn to a method of detecting a nucleic acid molecule that encodes a heparan sulfate 3-*O*-sulfotransferase 5 polypeptide in a biological sample containing nucleic acid material, the method comprising: (i) hybridizing the nucleic acid molecule, of a nucleic acid molecule encoding an isolated and purified biologically active heparan sulfate 3-*O*-sulfotransferase 5 polypeptide, under stringent hybridization conditions to the nucleic acid material of the biological sample, thereby forming a hybridization duplex; and (ii) detecting the hybridization duplex.

IX. Claims 19-25, drawn to an assay kit for detecting the presence of a heparan sulfate heparan sulfate 3-*O*-sulfotransferase polypeptide in a biological sample, the kit comprising a first antibody capable of immunoreacting with a polypeptide of claim 1.

X. Claims 26-28, drawn to a method of screening candidate substances for an ability to modulate heparan sulfate 3-*O*-sulfotransferase 5 polypeptide biological activity, the method comprising: (i) establishing test samples comprising a heparan sulfate 3-*O*-sulfotransferase 5 polypeptide; (ii) administering a candidate substance to the test samples; and (iii) measuring the interaction, effect, or combination thereof, of the candidate substance on the test sample to thereby

determine the ability of the candidate substance to modulate heparan sulfate 3-*O*-sulfotransferase 5 polypeptide biological activity.

XI. Claim 29, drawn to a recombinant cell line suitable for use in the method of claim 28.

XII. Claims 30-34, drawn to a method of modulating heparan sulfate 3-*O*-sulfotransferase 5 polypeptide biological activity in a vertebrate subject, the method comprising the step of administering to the vertebrate subject an effective amount of a substance capable of modulating activity of a heparan sulfate 3-*O*-sulfotransferase 5 polypeptide in the vertebrate subject to thereby modulate heparan sulfate 3-*O*-sulfotransferase 5 biological activity in the vertebrate subject.

XIII. Claims 35-36, drawn to a composition comprising an effective amount of a modulator of a biological activity of a heparan sulfate 3-*O*-sulfotransferase 5 polypeptide, and a pharmaceutically acceptable diluent or vehicle.

XIV. Claims 37-42, drawn to a method for modulating transfer of sulfate to the 3-OH position of a glucosamine residue of heparan sulfate in a vertebrate subject, the method comprising introducing to a target tissue producing heparin sulfate in the vertebrate subject a construct comprising a nucleic acid sequence encoding a heparan sulfate 3-*O*-sulfotransferase 5 gene product operatively linked to a promoter, wherein production of the heparan sulfate 3-*O*-sulfotransferase 5 gene product in the target tissue results in modulation of transfer of sulfate to the 3-OH position of a glucosamine residue of heparan sulfate.

XV. Claims 43-53, drawn to a method for modulating production of 3-*O*-sulfated heparan sulfate in a vertebrate subject, the method comprising introducing to a target tissue comprising cells producing heparan sulfate in said vertebrate subject a construct comprising a nucleic acid sequence encoding a heparan sulfate 3-*O*-sulfotransferase 5 gene product operatively linked to a promoter, wherein production of the heparan sulfate 3-*O*-sulfotransferase 5 gene product in the target tissue results in modulation of production of 3-*O*-sulfated heparan sulfate.

XVI. Claims 54-60, drawn to a method for increasing the efficacy of treating a disorder using a virus vector for delivering therapeutic nucleic acid molecules to the cells of a subject, comprising administering to the subject a construct comprising a nucleic acid sequence encoding a heparan sulfate 3-*O*-sulfotransferase 5 gene product operatively linked to a promoter prior to administration of the virus vector, wherein production of the heparan sulfate 3-*O*-sulfotransferase 5 gene product in the cells results in increased expression of 3-*O*-sulfated heparan sulfate, and wherein the 3-*O*-sulfated heparan sulfate is an entry receptor for the virus vector.

3. The inventions listed as Groups I-XVI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Applicant's claims encompass multiple inventions and do not have a special technical feature which link the inventions one to the other, and lack unity of invention. The common

technical feature in all groups, as stated in claim 1-2, is a polypeptide encoded by SEQ No.1 or a nucleic acid sequences having greater than 90% sequence identity to SEQ No.1, wherein the polypeptide is preferentially a heparan sulfate 3-*O*-sulfotransferase 5 (3-OST-5) polypeptide or a polypeptide which is biological equivalent of the polypeptide set forth in SEQ ID No. 2. However, this common technical feature cannot be a special technical feature under PCT Rule 13.2 because the feature is shown in the prior art.

Myette et al. purified and characterized human heparan sulfate 3-O-sulfotransferase-1 (Myette et al. Expression in Escherichia coli, purification and kinetic characterization of human heparan sulfate 3-O-sulfotransferase-1 (3-OST-1). *Biochem Biophys Res Commun.* 290(4): 1206-13, 2002). Furthermore, Xia et al isolated Heparan sulfate 3-O-sulfotransferase isoform 5 (3-OST-5) by probing the non-redundant data base of National Center for Biotechnology Information with the deduced amino acid sequence of human 3-OST-1 (accession number AF033827) (Xia et al, Heparan sulfate 3-O-sulfotransferase isoform 5 generates both an antithrombin-binding site and an entry receptor for herpes simplex virus, type 1. *J Biol Chem.* 2002 Oct 4;277(40):37912-9. Epub 2002 Jul 23).

Inventions of the Groups I-XVI are patentably distinct each from the other because Groups I-V, IX, XI, XIII are directed to products: a polypeptide for Group I, an antibody for Group II, an isolated and purified nucleic acid molecule for Group III, a recombinant host cell for Group IV and XI, a transgenic non-human animal for Group V, an assay kit for Group IX, a composition XIII whereas Groups VI-VIII, X, and XII, XIV-XVI are directed to different methods.

The products of Groups I-V, IX, XI, and XIII are distinct one from each other because they are different in structures, functions, and components of the product (Groups I-V, IX, XI, XIII) or different in molecules versus a cell or an organism (Groups I-III, versus Groups IV-V, XI).

The methods of Groups VI-VIII, X, and XII, XIV-XVI are distinct one from each other because they comprise different steps and technical considerations: to a method of, producing an antibody immunoreactive with a heparan sulfate 3-*O*-sulfotransferase 5 polypeptide (Group VI), A method of detecting a heparan sulfate 3-*O*-sulfotransferase polypeptide (Group VII), detecting a nucleic acid molecule that encodes a heparan sulfate 3-*O*-sulfotransferase 5 polypeptide in a biological sample containing nucleic acid material (Group VIII), screening candidate substances for an ability to modulate heparan sulfate 3-*O*-sulfotransferase 5 polypeptide biological activity (Group X), a method of modulating heparan sulfate 3-*O*-sulfotransferase 5 polypeptide biological activity in a vertebrate subject (Group XII), a method for modulating transfer of sulfate to the 3-OH position of a glucosamine residue of heparan sulfate in a vertebrate subject (Group XIV), a method for modulating production of 3-*O*-sulfated heparan sulfate in a vertebrate subject (Group XV), and a method for increasing the efficacy of treating a disorder using a virus vector for delivering therapeutic nucleic acid molecules to the cells of a subject (Group XVI).

Groups I-V, IX, XI, XIII are distinct from Groups VI-VIII, X, and XII, XIV-XVI because the intrinsic characteristics of the products of Groups I-V, IX, XI, XIII are not obvious over the steps of methods of VI-VIII, X, and XII, XIV-XVI.

The search of the above listed Groups I-XVI is distinct one from each other and not co-extensive and thereby presents search burdens on the examiner.

4. Because these inventions are independent or distinct for the reasons given above and the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

5. The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicants traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Notice of Possible Rejoinder

6. The examiner has required restriction between products and process of using the products claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims

directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

7. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent examiner, Ram Shukla, can be reached on (571) 272-0735. The fax number for TC 1600 is (571) 273-8300. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to Dianiece Jacobs whose telephone number is (571) 272-0532.

Wu-Cheng Winston Shen

RAM R. SHUKLA, PH.D.
SUPERVISORY PATENT EXAMINER

Wu-Cheng Winston Shen, Ph. D.
Patent Examiner
Art Unit 1632